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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,120	01/12/2001	Sarah S. Bacus	MBHB01-033	1979

20306 7590 06/03/2002

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EXAMINER

GABEL, GAILENE

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 06/03/2002

4

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/760,120

Applicant(s)

BACUS, SARAH S.

Examiner

Gailene R. Gabel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 January 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims Under Examination

1. Claims 1-14 are pending and under examination.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings in this application are also objected to by the Draftsperson (see PTO-948 attached). Correction is required.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

A. Correction of Informalities -- 37 CFR 1.85

New formal drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the Notice of Allowability. Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136(a) or (b) for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be

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allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

C. Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step b) has no antecedent basis in reciting, "the optical density".

Claim 1, step d), line 2-3 lacks clear antecedent support in reciting "the target protein " in the second occurrence of the phrase in the claim because the first occurrence refers back to the target protein in the sample but the second occurrence of "the target protein" is not distinctly defined. Perhaps, Applicant intends to recite, "the known amounts of the target proteins in the first and second control pellets using the calibration curve".

Claim 3 is indefinite in reciting, "EGFR", "AKT", "MAP". Acronyms or abbreviations must be recited at least one time in a set of claims.

Claim 5 is indefinite in reciting, "consistent" because the term "consistent" is a subjective term that lacks a comparative basis for defining its metes and bounds.

Claim 7 is indefinite in reciting, "ELISA". Acronyms or abbreviations must be recited at least one time in a set of claims. See also claim 14.

Claim 8 lacks clear antecedent support in reciting, "the target protein is normalized to the amount of protein in the cell pellet" because it is unclear as to which amount of target protein, i.e. from the sample or known control cell pellet, is being normalized. Further, it is unclear how the "target protein" relates to the "(amount of) protein" in a cell pellet. See also claims 9-10.

Claim 11 is vague and indefinite in reciting, "optical density of the staining in the cells". Perhaps, Applicant intends to recite, "optical density of the stained cells".

Claim 12 lacks clear antecedent basis in reciting, "the stained biological sample. Perhaps Applicant intends "the stained cells in the biological sample".

Claim 12 is confusing and lacks antecedent support in reciting, "a multiplicity of stains used to stain the cells" because in claim 1, staining of the cells in the biological sample, the first control pellet, and the second control pellet appears to be performed only using one stain, i.e. detectably labeled antibody, directed against the target protein in question.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

4. Claims 1-11 and 13-14 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Slamon et al. (US 5,846,749).

Slamon et al. disclose a method of determining expression level of target protein in cells from a homogeneous cell population by immunohistochemically staining the cells in order to provide a spectrophotometric signal capable of quantitation by computerized image analysis. Slamon et al. use immunohistochemically stained control cell pellets (standards) with the method to relate the spectrophotometric signal to the quantitative amount of target protein on an individual cell basis. (See column 2, lines 17-28 and line 58, bridging to column 3, line 27). Specifically, Slamon et al. use two or more control cell pellets (cell compositions) each having different amounts of target protein. The control cells express a consistent amount of the target protein in different levels within a desired range (see column 4, lines 14-35). All values obtained from the control cell pellets may be normalized based on the values obtained in direct comparison of values (see column 4, lines 42-44). Slamon et al. disclose staining the cells using detectably-labeled antibodies directed against the target protein, i.e. surface membrane protein receptor, organelle protein, including glycoproteins, etc. (see column 2, lines 29-51). Various labels for immunohistochemical staining include fluorescers and enzymes which produce a product which absorbs light or fluoresces (chromagen)

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(see column 3, lines 34-54). In the method, Slamon et al. specifically disclose immunohistochemically assaying the sample and control cell pellets at the same time so as to obtain a direct correlation between the amount of protein present in the cells per cell and the optical density signal observed with the immunohistochemical staining. Thereafter, Slamon et al. prepare a quantitation curve relating the optical signal observed with the immunohistochemical staining and the amount of target protein present in the pellet cells. Alternatively, Slamon et al. disclose using a standard curve obtained from a plurality of determinations where the curve is determined by at least two or more assay determinations. Assays used include enzyme linked immunosorbent assay (ELISA). The signal obtained from the sample is related to the concentration curve relating signal to concentration, to concentration of the target protein with known amounts of the protein in the control cell pellets. Slamon et al. teach application of the method in determining malignant cell expression in an animal, i.e. Her2/neu overexpression (see columns 7-8).

5. Claims 1-3, 6, and 11-13 are rejected under 35 U.S.C. 102(e) as being anticipated by McNamara et al. (US 6,007,996).

McNamara et al. disclose a method of in situ analysis of biological sample by staining the sample with four different immunohistochemical stains and collecting spectral data wherein each spectrum is associated with a target protein, i.e. cytological marker, that is individually detectable. McNamara et al. use optical filters, i.e. filter-based spectral data collection device, so that each signal from each of the multiplicity of

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stains used to stain the sample is obtained (see column 31, lines 61-67, column 35, lines 27-38, and column 37). The immunohistochemical stain comprises detectably labeled antibodies, i.e. anti-Her-2/neu antibody (multiple cancers), which bind target proteins, i.e. Her-2/neu, within or on the cells (see column 36, lines 34-42 and columns 40-41). Detectable labels are listed in column 38, lines 36 to column 39, line 40.

McNamara et al. specifically disclose immunohistochemically staining control cells (calibration or reference material) which are simultaneously co-stained with the biological sample, obtaining optical density measurements, and comparing results therebetween (see column 38, lines 4-24).

6. No claims are allowed.

Information Disclosure Statement

7. The Information Disclosure Statement (PTO-1449) filed March 22, 2002 (Paper number 4) is acknowledged. The following references, 1) DiGiovanna, 1999, PPO Updates: Princ. Practice Oncol. 13: 1-9, 2) Shak, 1999, Semin. Oncol. 26: 26:60-70, and 3) Sliwkowski et al., 1999, Semin. Oncol. 26:60-70, were not considered because no copy of each reference was provided. Specifically, 37 CFR 1.98(a)(2) requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed.

Remarks

8. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

Bacus (US 5,202,931) discloses an image analysis system for quantitative immunohistochemical assay of nuclear protein in a cell populations. Measurements of optical density values of stained receptor areas yield an intensity value related to the quantity the target protein (see Abstract).

Johnston et al. (US 5,998,151) disclose determining expression level of target protein in a tissue sample to evaluate chemotherapeutic treatment.

Garini et al. (US 6,165,734) disclose a method of in situ analysis of a biological sample by immunohistochemical staining cells in the sample and using spectral data collection device to collect data attributed to the specific immunohistochemically stained proteins in the cells.

Van Diest et al. (Analytical Cellular Pathology, 1991) teach a method of quantitating HER-2/neu oncoprotein overexpression in invasive breast cancer by image analysis.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday 6:00 AM to 3:30 PM and alternate Fridays.


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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
May 27, 2002




CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1899~~ /641